

Role of autonomous androgen receptor signaling in prostate cancer initiation is dichotomous and depends on the oncogenic signal.

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Public Summary:

The steroid hormone signaling axis is thought to play a central role in initiation and progression of many hormonally regulated epithelial tumors. It is unclear whether all cancer-initiating signals depend on an intact hormone receptor signaling machinery. To ascertain whether cell autonomous androgen receptor (AR) is essential for initiation of prostate intraepithelial neoplasia (PIN), the response of AR-null prostate epithelia to paracrine and cell autonomous oncogenic signals was assessed in vivo by using the prostate regeneration model system. Epithelial-specific loss of AR blocked paracrine FGF10-induced PIN, whereas the add back of exogenous AR restored this response. In contrast, PIN initiated by cell-autonomous, chronic-activated AKT developed independent of epithelial AR signaling. Our findings demonstrate a selective role for AR in the initiation of PIN, dependent on the signaling pathways driving tumor formation. Insights into the role of hormone receptor signaling in the initiation of epithelial tumors may help define this axis as a target for chemoprevention of carcinomas.

Scientific Abstract:

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